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Emotion regulation and premedication success relationship in children who underwent general anesthesia

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Background/aim: This study aims to investigate the relationship between emotion regulation characteristics and the efficacy of midazolam premedication.

Materials and methods: Sixty-three children, aged 3 to 8 years old, with tonsillectomy and/or adenoidectomy and taking premedication with midazolam (Group 2) or without premedication (Group 1), were included in this study. The behavioral and emotional status of the children was evaluated with the Conners Parent Rating Scale-48 (CPRS-48) and Emotion Regulation Checklist (ERC). Age, sex, body weight, response to intravenous (IV) cannulation and mask, hemodynamic data, preoperative sedation scores [Wilton Sedation Scale (WSS)], postoperative pain intensity [Objective Pain Scale (OPS)], and emergence agitation (EA) level [Pediatric Anesthesia Emergence Delirium (PAED)] were recorded.

Results: A total of 90.6% patients were quiet and sleepy in Group 2, and 25.8% in Group 1. The mean scores of OPS and PAED were higher in Group 1, and the percentage of patients with PAED score of >10 was 51.6% in Group 1 and 18.8% in Group 2 ($P < 0.05$). In Group 1, a significant correlation was found between PAED scores and WSS and the subfactors of the CPRS-48 ($P < 0.05$). A correlation was found between WSS and subfactors of ERS in Group 1 ($P < 0.05$).

Conclusion: The incidence of anxiety and postoperative EA is increased in children with emotion regulation disorder, and midazolam premedication reduced the frequency of EA.

Key words: Children, midazolam, emergence agitation, emotion regulation

I. Introduction

Agitation is a frequent complication during the recovery period of anesthesia in children. Termed as emergence agitation (EA), it often presents with mental confusion, disorientation, crying, irritability, and severe restlessness (1). Premedication with pharmacological agents, mainly benzodiazepines, is a common procedure in children to enable preoperative sedation and reduce the frequency of EA (2). Midazolam has been widely used thanks to its rapid onset of action, minimal side effects, and rapid emergence characteristics (3).

EA is associated with several factors such as age, high anxiety level, airway obstruction, severe pain, and rapid recovery from anesthesia. To date, a correlation has been shown between the postoperative agitation and anxiety level of the parents, mood, and behavioral and sleep disturbances in children (1). Self-conscious stunted children with a lack of concern, children who do not possess improved adaptive abilities, and children who previously experienced adverse effects related to surgery or physicians are at increased risk (4).

Furthermore, emotions may affect decision-making, memory, interindividual relations, and behaviors. Emotional and behavioral disorders develop as a result of the transfer of mental and physical internal conflicts to behavior. Additionally, emotional and behavioral disorders may cause problems in family relations, social life, and school life, and can make the treatment complicated. Emotion regulation is the ability to change the intensity, characteristics, and duration of the emotional response of the individual to carry out an aim or to adapt to a social environment (5). Previous studies have demonstrated that inability in emotion regulation (ER) and emotional expression is correlated with behavioral problems (6). Furthermore, several studies have shown that ER disorder is an important factor that produces aggressive behaviors (7). There are studies investigating the relationship between ER disorder and anxiety disorders, demonstrating that each

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disorder increases the other (8). Keser et al. (9) reported that ER disorder significantly increased the incidence of diagnosis of attention deficit and hyperactivity disorder (ADHD) in children.

Moreover, the efficacy of sedative agents has been shown to be affected by personal factors such as mood (2). On the other hand, the relationships between ER and behavior disorder characteristics, the incidence of EA, and the success of premedication have not been clarified.

Therefore, in this study, we aimed to investigate the relationship between ER characteristics and the efficacy of premedication with midazolam by analyzing the success of sedation and the frequency of EA in children undergoing day-case surgery under general anesthesia.

2. Materials and methods

A total of 64 randomized selected children in the American Society of Anesthesiologists (ASA) I–II group, aged between 3 and 8 years, who underwent day-case tonsillectomy and/or adenoidectomy, were enrolled in the study. Written informed consent was obtained from each parent. The study protocol was approved by the Gazi University Clinical Research Ethics Committee. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Sixty-four children received either no premedication (Group 1, n = 32) or premedication with 0.5 mg kg^{-1} oral midazolam (Dormicum, Roche Müstahzarları Sanayi A.Ş., İstanbul, Turkey) (Group 2, n = 32). Anesthesia induction was achieved with 5 mg kg^{-1} Na- thiopental (Pental thiopental Na flacon, İbrahim Etem İlaç, İstanbul, Turkey) intravenously in patients given permission for intravenous (IV) access, and with 6% sevoflurane in 50%/50% O_2/air mixture in patients that did not receive permission. Anesthesia was maintained with sevoflurane in 1 ± 0.8 minimum alveolar concentration (MAC) values and remifentanil infusion following the administration of 0.6 mg kg^{-1} IV rocuronium bromide (Curon 50 mg/5 mL [Mustafa Nevzat, İstanbul, Turkey). Exclusion criteria were as follows: ASA III–IV, diagnosis of psychiatric disorders, use of drugs during recruitment, history of emergent procedures, and lack of research data. Age, sex, body weight, ASA classification, time of initiation and end of anesthesia, adaptation to mask placement and IV access, preoperative sedation levels [Wilton Sedation Scale (WSS)], drugs used during anesthesia induction and maintenance, hemodynamic data, postoperative pain [Objective Pain Scale (OPS)], and Pediatric Anesthesia Emergency Delirium (PAED) scores were recorded. To evaluate the behavioral and emotional status of the children, the Emotion Regulation Checklist (ERC) (10,11) and Conners Parent Rating Scale (CPRS-48) (12,13) were administered to the parents. The scales and subfactors were evaluated separately for each group and relations to the success of sedation and postoperative EA were evaluated.

The CPRS-48 is one of the most used behavioral scales in clinical and research settings for children suffering from neurodevelopmental disorders, and particularly for children with ADHD. This scale provides an interesting qualitative and quantitative picture of the child's emotional and behavioral attitude because it includes five subscales that assess conduct problems, learning problems, anxiety, impulsive/hyperactive behavior, and psychosomatic feelings (13). The CPRS-48 scale consists of a total of 48 items, and the Attention Deficit Disorder Factor (ADDF), Hyperactivity Disorder Factor (HDF), Oppositional Defiant Disorder Factor (ODDF), and Behavior Deficit Factor (BDF) consist of 5, 4, 5, and 11 items, respectively.

The 24-item ERC taps into both the prevalent emotional expressiveness and the product aspect of ER; that is, it targets processes central to emotionality and regulation, including affect lability, intensity, valence, flexibility, and contextual appropriateness of expressiveness (11). The Lability/Negativity (LN) subscale comprises items representing a lack of flexibility, mood lability, and dysregulated negative affect. The REC subscale includes items describing situationally appropriate affective displays, empathy, and emotional self-awareness.

2.1. Statistical analysis

Statistical analysis was performed with SPSS 20.0 (IBM Corp., Armonk, NY, USA). Data were analyzed with the Mann–Whitney U test, and repeated hemodynamic data were analyzed with repeated measures analysis of variance and Bonferroni's correction test. Sex, ASA classification, type of surgery, WSS, permission for IV cannulation, response to mask placement, OPS, PAED, CPRS-48, and ERS were assessed with chi-square or Fisher's exact chi-square tests. The relations between the PAED and WSS, and between the ERS and CPRS-28, were evaluated with Pearson's correlation analysis. $P < 0.05$ was considered statistically significant.

3. Results

Thirty-two patients in Group 1 (no premedication) and 31 patients in Group 2 (0.5 mg kg^{-1} oral midazolam) were included in this study. One patient in Group 2 was excluded from the study due to lack of ERS and CPRS-48 data. No significant difference in age, sex, body weight, ASA risk group, type of surgery, duration of surgery and anesthesia, or hemodynamic data (systolic arterial pressure, diastolic arterial pressure, mean arterial pressure, heart rate, saturation of O_2) was observed between the groups ($P > 0.05$; Tables 1 and 2, Figure 1).

According to the WSS data, the percentage of patients who had agitation was 51.6% in Group 1, which was significantly higher than in Group 2 ($P < 0.001$). A total

Table 1. Demographic properties of Groups 1 and 2 [mean ± SD, min–max (n)].

	Group 1 (n = 31)	Group 2 (n = 32)	P
Sex (M/F)	20/11	22/10	0.722
Age (years)	5.97 ± 1.38 (4–8)	6.03 ± 1.49(3–8)	0.757
Body weight (kg)	22.59 ± 7.02 (12–37)	21.88 ± 5.37 (11–36)	0.869
ASA (I/II)	28/3	26/6	0.474

Table 2. Type of surgery, operation, and anesthesia time variables [n (%)] [mean ± SD, min–max].

	Group 1 (n = 31)	Group 2 (n = 32)	P
Operation			
Tonsillectomy (T)	2 (6.5)	5 (15.6)	0.076
Adenoidectomy (A)	13 (41.9)	19 (59.4)	
T + A	16 (51.6)	19 (59.4)	
Operation time (min)	36.55 ± 15.68 (15–70)	35.63 ± 13.49 (15–70)	0.950
Anesthesia time (min)	55.06 ± 16.81 (25–90)	54.75 ± 15.37 (35–90)	0.890

of 25.8% of patients in Group 1 and 65.6% of patients in Group 2 were quiet (Figure 2).

The percentage of patients who had been given permission for IV cannulation and did not respond to the mask placement was significantly higher in Group 2 compared to Group 1 ($P < 0.001$). The induction agent was sevoflurane at a rate of 83.9% in Group 1 and Na-thiopental at a rate of 62.5% in Group 2 ($P < 0.0001$; Table 3).

The mean value of PAED was found to be higher in Group 1 compared to Group 2 ($P = 0.008$). The percentage of patients with postoperative PAED score of >10 was 51.6% in Group 1 and 18.8% in Group 2, indicating a statistically significant difference ($P = 0.006$; Table 4). The mean value of the OPS was found to be significantly higher in Group 1 ($P < 0.0001$).

Based on the psychiatric test results, a positive correlation was found between PAED and subfactors of CPRS-48 such as ADDF, ODD, and BDF ($r = 0.418$, $P = 0.019$; $r = 0.328$, $P = 0.036$; $r = 0.418$, $P = 0.019$, respectively). In Group 1, a negative correlation was found between WSS and subfactors of ERC, such as variability/negativism, and subfactors of CPRS-48, such as ADDF, ODDF, and BDF ($r = -0.335$, $P = 0.033$; $r = -0.353$, $P = 0.026$; $r = -0.335$, $P = 0.033$, respectively). In Group 2, no correlation was observed between WSS and subfactors of ERS and the total score of CPRS-48 and subfactor scores. In Group 2, no correlation was found between the PAED and subfactors of ERC and total CPRS-48 score and subfactor scores.

4. Discussion

The present study found that premedication with 0.5 mg kg^{-1} oral midazolam enabled preoperative sedation, increased the success of IV cannulation and the acceptance of mask placement, and significantly reduced the incidence of postoperative EA. Furthermore, a correlation was found between EA and attention deficit disorder, opposition disorder, and behavioral disorder in patients who had no premedication with midazolam.

The success of IV cannulation could enable induction with IV anesthetic agents and could prevent the use of inhalational agents (such as sevoflurane) at high MAC values during induction, which causes postoperative agitation. On the other hand, anxiety, postoperative EA, and pain intensity were high in children with ER disorder, attention deficit, opposition, and behavioral disorders. Preoperative anxiety and postoperative EA were lower in children who had had premedication with midazolam and psychiatric disorders.

The incidence of negative behaviors during the postoperative period has been shown to be 3.5-fold higher in children with high anxiety levels during the preoperative period compared to children with low levels of anxiety (14). Thus, sedative premedication has been suggested to be beneficial in reducing preoperative fear and anxiety (15). Many previous studies have demonstrated that midazolam, which is frequently used for premedication in children, is an effective and reliable agent for premedication (3).

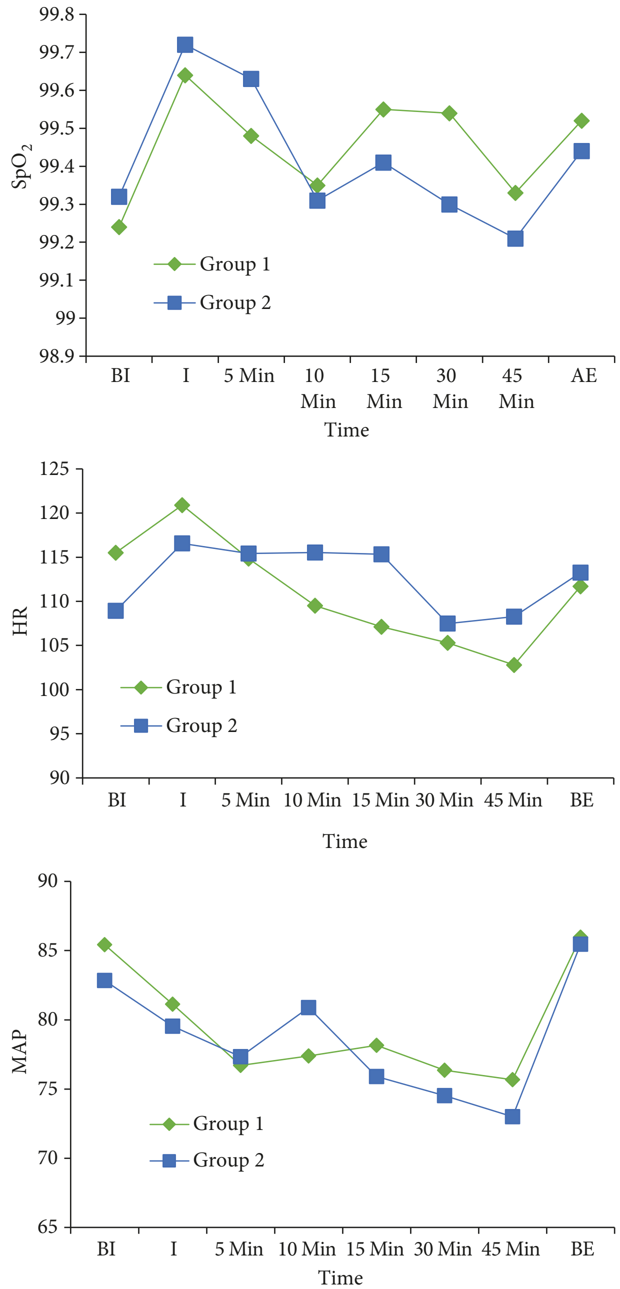

Figure 1. Hemodynamic variables (MAP: mean arterial pressure, HR: heart rate, SpO_2: saturation of oxygen) in Groups 1 and 2. *P < 0.05 compared with Group 1.

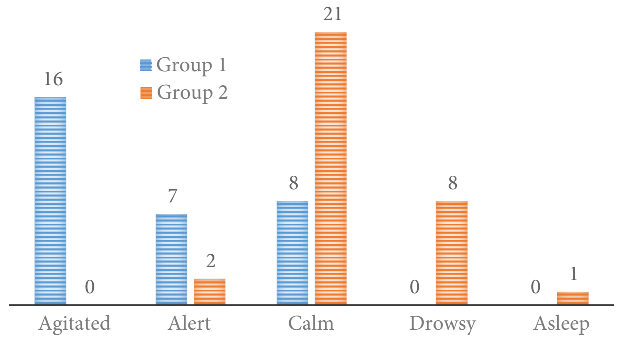

Figure 2. WSS scores in Groups 1 and 2. *P < 0.05 compared with Group 1.

In the study of Kain et al. (16), which investigated the relationship between preoperative anxiety and social adaption, cognitive abilities, and other personal features, preoperative anxiety was high in self-conscious noncommunicative children, children with adaptation difficulty due to high IQ, children who had previous negative experiences related to physicians and hospital visits, and children of single or divorced parents (16).

Furthermore, mood features are related to behavior and emotion, and a child's mood is the key determinant of the reaction to stressful conditions (17). Buss et al. (17) defined four types of moods in children (emotiveness, activity, socialism, and irritability) and developed the Emotionality, Activity, Sociability, Impulsivity (EASI) scoring for mood assessment of children. Kain et al. (15) assessed anxiety levels with a visual analog scale (VAS) in the waiting room during the preoperative period and separation from the family and reported that anxiety levels were high in self-conscious and hindered children (low EASI activity score). In the aforementioned study, the authors additionally reported that impulsive children (high EASI impulsive score) had high levels of separation anxiety during the 2-week postoperative period. Finkley et al. (18) assessed mood features with EASI and compared the level of anxiety in children who had 0.5 mg kg^{-1} oral midazolam or a placebo during induction. The authors found that the children with high levels of anxiety experienced more benefits from premedication with midazolam. Furthermore, no beneficial anxiolytic effect was observed in children with high EASI impulsivity scores who had premedication with midazolam during induction. Thus, they reported that midazolam might be contraindicated during preoperative medication in children with impulsive features. The present study found that although EA was more frequent in children with attention deficit disorder, opposition disorder, and behavioral disorder, EA was observed less frequently in patients who had premedication with midazolam. In addition, Kain et al. (19) investigated blood levels of midazolam, anxiety levels, and mood features with EASI to analyze the possible relationship among them. The Yale Preoperative Anxiety Scale (mYPAS) score was higher than 72.9 in 14.1% of the children, who were defined as midazolam-nonresponsive patients. No difference was found in the blood levels of midazolam in midazolam-responsive and -nonresponsive groups. The midazolam-nonresponsive group was significantly younger (below

Table 3. Reaction of IV cannulation, anesthetic agents used for induction, and mask response data in Groups 1 and 2 [n (%)].

		Group 1 (n = 31)	Group 2 (n = 32)	P
IV cannulation reaction	Allowed	5 (16.1)	20 (62.5)*	χ^2 = 14.14 <0.0001
	Not allowed	26 (83.9)	12 (37.5)*	
Induction agents	Sevoflurane	26 (83.9)	12 (37.5)*	χ^2 = 14.97 <0.0001
	Pentothal	5 (16.1)	20 (62.5)*	
Mask response	Unresponsive	5 (16.1)	27 (84.4)*	χ^2 = 29.34 <0.0001
	Responsive	26 (83.9)	5 (15.6)*	

*P < 0.05 compared with Group 1.

Table 4. PAED data in Groups 1 and 2 [n (%)] [mean ± SD, min–max].

PAED scores	Group 1 (n = 31)	Group 2 (n = 32)	P
PAED scores (mean)	11.71 ± 3.12 (7–19)	9.50 ± 2.23* (3–14)	0.008
PAED scores <10 / >10 (%)	15 (48.4) / 16 (51.6)	26 (81.2) / 6 (18.8)*	χ^2 = 7.48 0.006

*P < 0.05 compared with Group 1.

the age of 4) and their EASI emotionality subfactor scores were significantly higher. The authors recommended increasing the dose of midazolam or using midazolam combined with other nonpharmacological methods in midazolam-nonresponsive younger and emotive children, although midazolam is an effective anxiolytic agent for most children.

Przybylo et al. (20) used the Child Behavior Check List (CBCL) to evaluate preoperative behaviors, and the Child-Life Specialist Test to evaluate the social environment of the children and the psychiatric history of their families. Postoperative behavioral changes in patients that had standard premedication and anesthesia were categorized by using the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV) criteria. In the aforementioned study, postoperative behavioral changes were observed at a rate of 44% and delirium was observed at a rate of 20%. No correlation was found between postoperative behavioral changes, delirium, and CPRS scores.

Isik et al. (21) evaluated the relationship between mood and behavioral problems and the success of sedation with midazolam. The Short Temperament Scale for Children (STSC) and the Revised CPRS: Long Form (CPRS-R:L) were administered, and the level of sedation was evaluated with the Houpt Sedation Rating Scale. Sedation was successful in 78.3% of children and unsuccessful in 21.6%. In the aforementioned study, STSC-inflexibility (behavioral inflexibility) and CPRS-R:L psychosomatic subfactor were significantly correlated with the success of sedation. The study reported that children with behavioral disorders, such as behavioral inflexibility, might be more prone to experiencing unsuccessful sedation in premedication with midazolam.

In the current study, the ERC and CPRS-48 were used to evaluate emotional status and behavioral characteristics. In Group 1, a positive correlation was found between the PAED and CPRS-48 (ADDF, ODDF, and BDF), and a negative correlation was found between the WSS and CPRS-48 (ADDF, ODDF, and BDF) and between the WSS and ERS-LN. In Group 2, no correlation was found between WSS and PAED and ERS and CPRS-48. In the current study, the increase in the incidence of anxiety and postoperative EA in children with ER disorder, attention deficit disorder, opposition disorder, and behavioral disorder was statistically significant. The absence of correlation in the group that had premedication with midazolam suggested that midazolam enables sedation and reduces the incidence of postoperative EA in children with psychiatric problems.

The absence of sevoflurane induction with mask in children given permission for IV access could impact the results of this study. Therefore, anesthesia induction with two different methods and absence of evaluation of blood midazolam levels constitute the limitations of our study.

In conclusion, although postoperative EA is seen more frequently in children with attention deficit, opposition, and behavioral disorders, preoperative premedication with 0.5 mg kg^{-1} midazolam decreases the incidence of EA in these children. In this context, researchers should examine the ER characteristics of the child to determine the intensity of EA as with anesthetic agents.

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